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Happy 40th, NIH Shared Instrumentation Program! The NIH Shared Instrumentation Grant Program Embraces a Promising Future

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ABSTRACT

The National Institutes of Health (NIH) offers many types of funding programs and opportunities to support biomedical research. The best known of these programs, the NIH Research Project Grant Program, or R01, supports investigator-initiated research projects. Another well-known funding mechanism is the NIH Shared Instrumentation Grant Program, also known as SIG or S10. This year marks the S10's 40th anniversary. To commemorate this triumphant milestone and a successful 40 years, let's first review how this legendary and highly impactful program started.

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Hallmarked by integrated-circuit and general-purpose computer microprocessors, the digital revolution of the second half of the 20th century led to a boom of biomedical and biotech industries in the 1970s and 1980s. The fast growth of modern biomedical technologies—such as nuclear magnetic resonance, computerized axial tomography, mass spectrometry, and electron microscopy—quickly rendered existing biomedical instruments behind or even obsolete. The inflation of the late 1970s, however, drove the costs of state-of-the-art instruments to skyrocket. As several reports[1],[2],[3],[4] indicate, the economic difficulties and reduced federal funding during the late 1970s resulted in the deterioration of scientific instruments being used in US institutions. It also underscored an unmet need for modern biomedical research instruments, particularly for those in the intermediate and high-end price range. Researchers across the nation and NIH extramural administrators began discussing ways to mitigate this major challenge to biomedical science and leverage rapid technology development.

Dr. Marvin Cassman, who served as a Section Chief at the National Institute of General Medical Sciences (NIGMS), was one of the first individuals to recognize the need for the NIH to modify its programs to fund the newest and most advanced instruments for biomedical research. Like other NIH units, the primary support for scientific equipment at that time was through R01s, which were designed to support research activities and were inadequate to support the purchase of expensive research equipment. To provide NIGMS grantees access to cutting-edge instrumentation, Dr. Cassman created a program—modeled after the National Science Foundation's Chemistry Research Instruments Program (now the Chemistry Research Instrumentation and Facilities Program) that had existed since the 1950s—to fund instruments on a shared-use basis. In the *NIH Guide for Grants and Contracts* published on January 19, 1979, NIGMS issued a new funding opportunity announcement (FOA) to support the purchase of a single analytical instrument in the price range of \$40,000 to

\$150,000. In this FOA, NIGMS requested that the instrument be used by at least 2 projects within NIGMS-funded programs. The new FOA also required that at least one-half of the core user group hold NIGMS research grants and mandated that the core user group account for at least 75% of the instrument use time. Although this NIGMS program was soon discontinued because of a lack of eligible applicants, these requirements continue to be the cornerstones of the S10 Program today.

Around the same time, Dr. Marjorie Tingle, then a Program Officer in the Biomedical Research Support (BRS) Branch in the Division of Research Resources (DRR) within the NIH Office of the Director, also saw the need for a simpler and more suitable mechanism than R01s to help as many NIH-funded researchers as possible to purchase costly instruments. At that time, the DRR used a noncompetitive BRS Grant (BRSG) Program to provide general research support funds to more than 500 institutions in the United States, which included health professional schools, graduate schools, hospitals, and research organizations. Dr. Tingle realized that by leveraging the broad legislative authority and the administrative structure of the BRSG program, a new competitive grant mechanism could be created to fund the purchase of modern instruments. Using her experience in concept development and program implementation obtained during 2 BRSG subprograms (the Biomedical Research Development Grant and the Minority High School Student Research Apprentice Program), Dr. Tingle developed the outlines of a new instrument program under the supervision of Dr. Thomas G. Bowery. This new program incorporated key elements of both the BRSG program (1-year awards, direct costs only, an advisory committee, placement of the instrument in central facilities) and the NIGMS program (core user group must use the instrument for 75% of the usage time). Eventually, the BRS advisory committee endorsed the concept clearance, and the DRR Council and the NIH Directorate all approved the program. The Division of Research Grants, the predecessor of the NIH Center for Scientific Review, also agreed to review applications in special instrument-specific study sections. Finally, the new FOA for BRS Shared Instrumentation Grants program was published in the *NIH Guide for Grants and Contracts* on June 26, 1981, announcing that a new NIH funding mechanism for supporting midrange cost instrumentation had been established. Designated as the S10 Program, this BRS Shared Instrumentation Grants program vastly expanded the spectrum of NIH investigators who could apply for instrument funding.

From the start, the S10 Program was designed to support and complement, not compete with, other NIH funding mechanisms, such as investigator-initiated research grants, program projects, and center grants. The pilot BRS Shared Instrumentation Grants program was provided a budget of \$3.7 million for 1982 to fund the shared use of cutting-edge instruments to rapidly advance biomedical research and benefit all NIH-supported researchers. “Of all of the substantial and important programs I have launched in my NIH career, the S10 Program was the most impactful,” said Dr. Tingle, who continues to express great pride in the S10 Program, even 10 years after retiring from the NIH.

The first S10 Program supported the purchase of instruments with a price range between \$75,000 and \$250,000 per instrument or system. After the first FOA was published, more than 200 applications were submitted,

showing an overwhelming enthusiasm and significant need on the part of the scientific research community. The budget was barely enough to award the top 23 most meritorious S10 applications, representing an 11% success rate, a number that was significantly lower than the success rates seen for other types of funding programs at the time. In subsequent years, the annual budgets progressively increased from \$3.7 million in 1982 to \$15 million, \$20 million, and \$31 million in 1983, 1984, and 1985, respectively, with success rates growing from 11% to 57%, 69%, and 76%, respectively (Figure 1). The overall success of the early S10 Program did not go unnoticed. The program was featured in the April 1985 edition of *Bio/Technology* (now the *Journal of Nature Biotechnology*).[5]

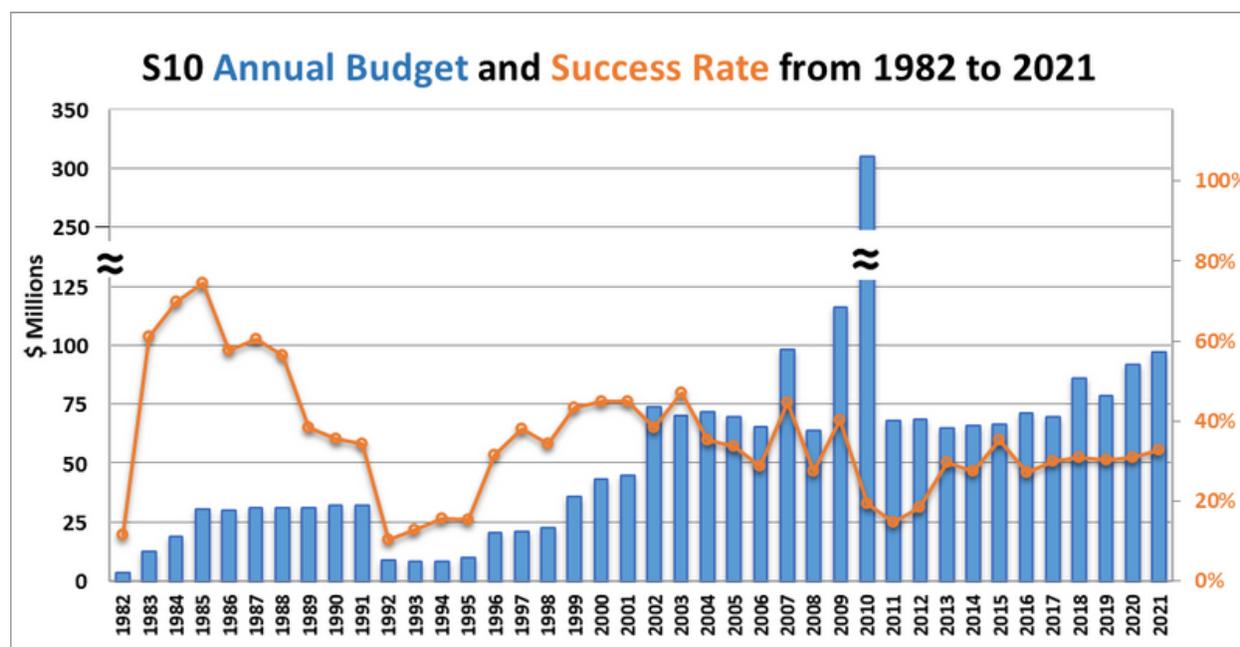


Figure 1

The overall annual budget and success rate for S10 Programs between 1982 and 2021.

Dr. Susan Weintraub was one of the 23 successful recipients of the first round of S10 awards in 1982. A Professor in the Department of Biochemistry and Structural Biology at The University of Texas Health Science Center at San Antonio (UTHSCSA), Dr. Weintraub has been the Director of the institutional Mass Spectrometry Core Laboratory since 1979. Dr. Weintraub was named a Fellow of the American Association for the Advancement of Science in 2017 for her pioneering work in the use of mass spectrometry to solve biomedical problems and for service to the scientific community. In 1981, Dr. Weintraub was a junior faculty member when she submitted her first S10 application, entitled “Mass Spectrometry Facility.” The application requested purchase of a Finnigan MAT 212 mass spectrometer, which featured a double-focusing magnetic sector instrument fitted with sample introduction by gas chromatography, fast-atom bombardment, and a moving-belt liquid chromatography–electron impact ionization interface (Figure 2 and Figure 3). Having access to an advanced, state-of-the-art mass spectrometer that allowed “soft” ionization was essential for her collaborative research at that time, which focused on identification, characterization, and quantification of

platelet-activating factor.^[6] Funding of this S10 grant was the impetus for her long career in biomedical mass spectrometry and the success of the core laboratory at UTHSCSA. “Without the S10 Program, there would not be [the] me of today!” explained Dr. Weintraub. As a recipient of 9 S10 awards from the NIH during the past 4 decades, Dr. Weintraub has significant appreciation for the S10 program. Dr. Weintraub was also one of the most recent S10 award recipients, making her the only person who has received S10 awards across the program’s entire 40-year span.

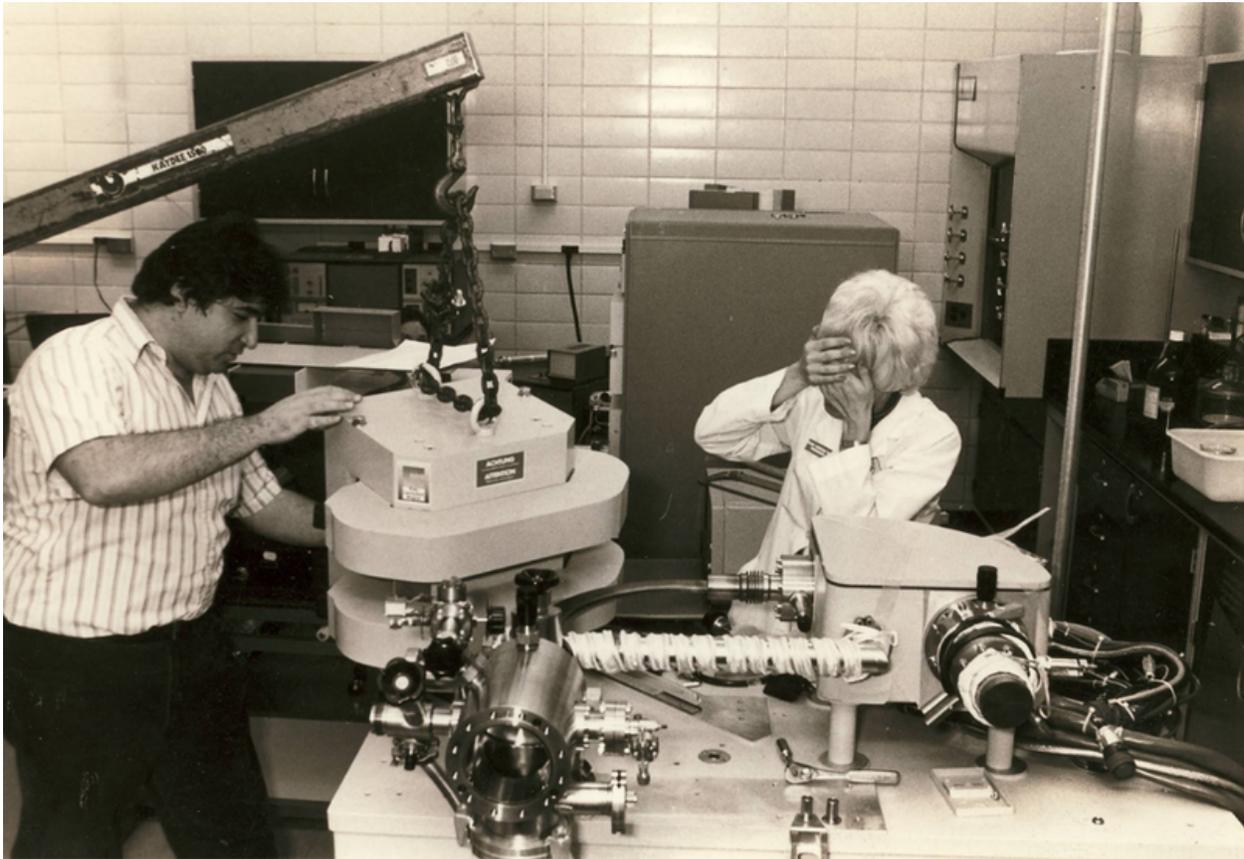


Figure 2

Dr. Susan Weintraub (right) was eagerly awaiting the debut of the Finnigan MAT212 mass spectrometer, acquired with her first S10 award, being installed by a technician (left) at The University of Texas Health Science Center at San Antonio in 1982. Dr. Weintraub was afraid to watch as an engine hoist was used to lower a heavy magnet into place. Photograph courtesy of Dr. Susan Weintraub.



Figure 3

A recent picture of Dr. Susan Weintraub working in her laboratory.
Photograph courtesy of Dr. Susan Weintraub.

Like Dr. Weintraub in her earlier years, many new researchers have received support from the S10 Program that has not only enabled their research but has also been essential for their career development and success. Instruments supported by S10 grants have contributed to numerous important scientific discoveries and helped

advance innovative research across a broad array of scientific disciplines. S10 recipients include Nobel laureates and members of the National Academies of Sciences, Engineering, and Medicine. Among the well-known scientists and S10 awardees is Dr. Jennifer A. Doudna, a Professor of Biochemistry and Molecular Biology at the University of California, Berkeley, who was a corecipient of the 2020 Nobel Prize in Chemistry for the development of the CRISPR-Cas9 method that reduces the time and work needed to edit genomic DNA. She received an S10 award for “Minstrel HTUV Gallery 700 Automated Crystal Growth and Imaging System” in 2013. Another S10 recipient, Dr. Elias A. Zerhouni, who served as NIH Director between 2002 and 2008 and is one of the few esteemed scientists who have been elected to the National Academies of Medicine and Engineering, received an S10 grant in 1993 to upgrade a magnetic resonance imaging system with an “Echo Planar 15T Gradient Probe” when he was the Chairperson of the Department of Radiology and Radiological Science at the Johns Hopkins University. Among the many beneficiaries of the S10 grant program is Dr. Charles Rice, a Professor in Virology at The Rockefeller University, who received the 2020 Nobel Prize in Physiology or Medicine with others for his co-discovery of the hepatitis C virus (HCV) while at the Washington University School of Medicine. His research has benefited from 4 S10 grants that supported his continuing research on HCV.

The numerous benefits of the S10 Program were evaluated by independent groups that considered researchers’ access to the state-of-the-art technologies and important advancements in science. The direct impact of the S10 Program on biomedical research was demonstrated in an independent, external assessment^[7], which found that 16,050 scientists nationwide had used the 1,487 instruments supported by S10 awards during the program’s first 11 years (fiscal years 1982 to 1993). The evaluation indicated that three-quarters of the S10 major users acknowledged the instruments were essential to their research.^[8] According to Dr. Tingle, “S10 gives thousands of NIH scientists access to the latest technologies which allowed them to ask questions they could not ask before, to make many new discoveries that might not have occurred, many of which have had a huge impact on science.”

Besides enabling cutting-edge research and helping scientists to advance their careers, S10-supported instruments—especially those installed in highly productive research and teaching institutions—help promote interdisciplinary collaboration, stimulate innovative ideas for product development, and facilitate the training of new users and the dissemination of technologies. Instruments installed in core facilities often produce high-volume and high-throughput services to support scientific research. Core facilities are usually operated with higher efficiency and better consistency in service quality as well as cost-effectiveness in operation and maintenance. In addition, the S10 Program ensures that core facilities operate efficiently with sophisticated technologies and specialized instrumentation, and these facilities provide opportunities to train staff and retain technical expertise for various user groups to benefit a broad range of research. These functions offer an alternative career path to academic routes for highly sought-after, highly specialized technical and managerial professionals. Both research-intensive laboratories and core facilities generate vibrant dynamics for scientific collaborations, idea exchanges, and knowledge sharing. The dynamic interactions that are enabled by the use of

these instruments in biomedical research further expand the user base, increasing demand for new and more advanced instruments, sustaining the healthy growth of the biomedical device industry and advancing biomedical research outside of academic research institutions.

During the past 40 years, the NIH has reviewed more than 17,000 S10 grant applications and issued approximately 5,500 S10 awards (Figure 4). The program has experienced its ups and downs. Dr. Tingle remembers the early 1990s as one of the most difficult times for S10s because the high demand for support far exceeded the available budget devoted to the program. Fortunately, at other times, the S10 Program received significant support. The American Recovery and Reinvestment Act (ARRA) of 2009, for example, appropriated \$300 million to the S10 Program, a substantial increase compared with the annual budget of \$60 million for the prior fiscal year (2008). The NIH appropriation under ARRA was made in response to the financial crisis in previous years and the deficient and aging infrastructure across the nation. The NIH was directed to develop strategies to help stimulate the economy and create and retain jobs while advancing biomedical research. In 2009, nearly 2,700 S10 applications were submitted to the NIH and reviewed in 34 peer-review study sections, resulting in more than 500 meritorious S10 awards to institutions in 42 states between fiscal years 2009 and 2010. Through the S10 Program, ARRA had a massive impact on a broad range of biomedical research areas and institutions in the United States by modernizing research infrastructure and instrumentation.

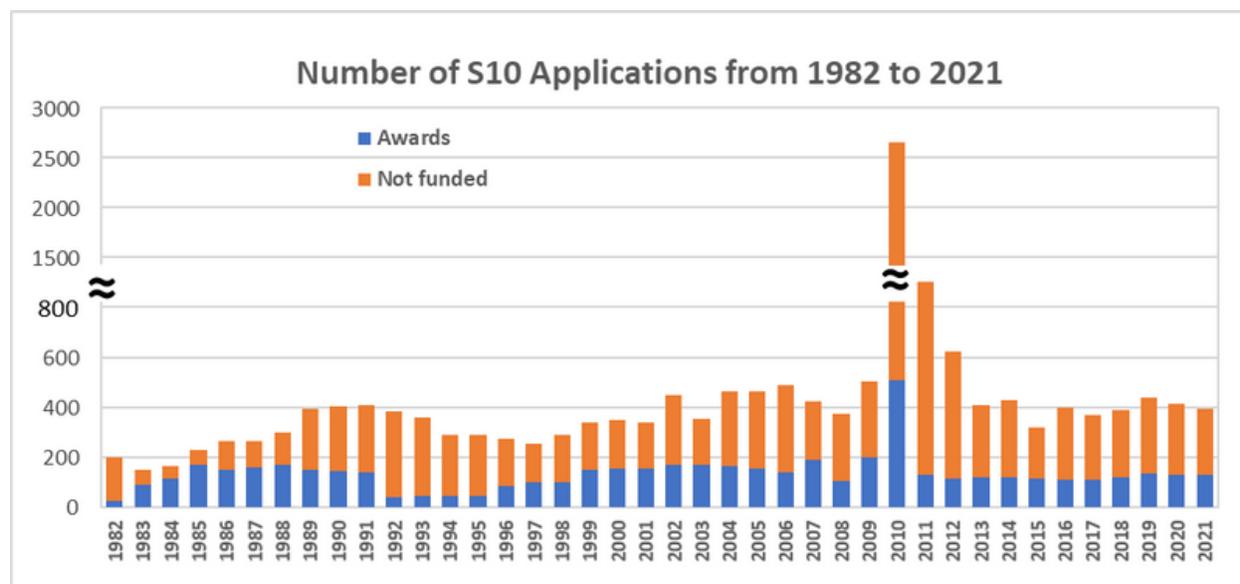


Figure 4

The number of applications and number of awards for the S10 Program between 1982 and 2021.

For the past 10 years, the S10 Program has been managed by extramural Program Directors in NIH's Office of Research Infrastructure Programs (ORIP), an office in the NIH Office of the Director. Under ORIP's management, the S10 Program has expanded rapidly. ORIP's first step toward expanding the S10 Program was

the addition of a new Basic Instrumentation Grants (BIG) Program to the 2 long-standing S10 FOAs—the Shared Instrumentation Grant program and High-End Instrumentation program, which was established in 2003. BIG is a limited award competition program allowing institutions to apply if they have not received an S10 award in the amount of \$250,000 or greater during the previous 3 years. ORIP also initiated a highly successful collaboration with NIGMS' Institutional Development Award (IDeA) Program, which has resulted in an increase in the annual S10 budget and awards in recent years. IDeA has been a congressionally mandated program since 1993 and is statutory by Title 42, The Public Health and Welfare (42 U.S.C. § 285k)[9] to support faculty development and institutional research infrastructure enhancement in states that historically have received low levels of support from the NIH. An example of an S10 grant awarded to an IDeA institution was the acquisition of a *Dynamic Imaging System* at the University of Idaho. The award funded the purchase of high-speed cameras and an automated focusing device, a key piece of instrumentation that was not accessible in the region, and fulfilled a critical research need at the institution by allowing researchers to conduct studies with cells, tissues, and small organisms to observe and document cellular and molecular changes associated with healthy neurobiology and diseased conditions. To the institution, the live-imaging microscope provides opportunities to study cells and small organisms while they are in motion, helping researchers to better understand how cells and organisms respond to environmental change or change in shape during development. Acquisition of the high-resolution imaging system significantly improved the infrastructure at the Optical Imaging Core in the University of Idaho's Institute for Bioinformatics and Evolutionary Studies. Modernization of the research infrastructure at the University of Idaho, which increased both the local research capacity and student exposure to research, was greatly welcomed.

The addition of IDeA funds made it possible to competitively award additional S10 grants to IDeA state institutions that otherwise might not have been funded. In addition to the collaboration with the IDeA program, ORIP formed collaborations with 4 other NIH Institutes, Centers, and Offices (ICOs) to co-fund S10 grants for shared use of instruments by investigators conducting research activities that meet the missions of those ICOs. These additional funds from other ICOs have boosted the S10 budget during the past several years (2018 to 2021), resulting in an overall success rate of 31% (averaged over 5 years). Another achievement for the ORIP S10 Program is the support of the Institutions of Emerging Excellence. These institutions are often situated in geographical areas with limited research resources but serve important roles in advancing biomedical research to address health care gaps and respond to health issues of special relevance to local populations from disadvantaged backgrounds.

During its 40-year history, the S10 Program has proven its value in strengthening the US biomedical research enterprise by supporting advanced instrumentation and infrastructure for a large number of biomedical research institutions and projects across the nation. The S10 Program allowed these institutions and their investigators to maintain modern scientific research operations and produce innovative research. Sharing expensive instruments among several investigators results in the most cost-effective investment of available research dollars—both for the research institution and the NIH—while increasing access to specific technologies for

investigators at both research-intensive institutions and institutions with limited resources. Furthermore, trainees and young investigators who have access to these shared instruments are given the opportunity to learn new techniques and expand their skill base. As the S10 Program requires substantial usage hours and shared use of the instruments among multiple projects, biomedical research is conducted efficiently and cost effectively. Thus, the Program increases the operational efficiency and competitiveness of our national biomedical research enterprise. This advantage is particularly valuable when the cost of an instrument is high. At its inception in 1982, the S10 Program was NIH's response to a major financial crisis. During the past 40 years, the S10 Program has served as a financial instrument to uphold our national biomedical research. It has shown that inaction during even minor economic downturns—such as in the early 1990s—results in hardship for NIH-supported researchers. It also shows that major investment—such as the ARRA appropriation for S10s—massively strengthens our nation's biomedical research infrastructure. With that funding, the S10 Program helped our nation's research engine navigate the global financial crisis of 2008. During recent economically challenging times, ORIP has addressed the growing demand for support of the instrument programs by leveraging its coalition-building capacity with other NIH ICOs.

The continued success of the S10 Program requires budgetary support based on an understanding of its value to sustain our nation's biomedical research. The synergistic and collaborative support from other NIH ICOs also will be essential to the effective stewardship of the S10 Program. In addition, the professionalism and dedication of NIH staff—including Scientific Review Officers, Program Directors, and Grant Management Officers who provide support for the program—are of paramount importance to the successful operation of the entire S10 funding process. Most important, the continued success of the S10 Program relies on the dedicated biomedical research investigators who contribute their time, knowledge, and energy to author S10 applications with the goal of securing NIH-funded shared instruments for their institution's research activities. Moreover, core facilities and other shared research resources will continue to serve a critical role in the dissemination of information, technologies, know-how, resources, and training.

Looking toward the future, ORIP will continue to evaluate the success of this program, monitor if researchers have appropriate access to modern equipment on a shared basis to conduct state-of-the-art research, and ensure that the S10 Program meets the evolving needs of NIH-funded investigators as well as the missions of NIH's diverse ICOs. Our vision is that the next 40 years of the S10 Program will support an even larger number and greater variety of shared instruments than the first 40 years, further advancing critical innovations and discoveries in biomedical research.

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